

WE CLAIM:

1. An isolated, mammalian, bone marrow-derived lineage negative hematopoietic stem cell population comprising endothelial progenitor cells in which at least about 50% of the cells include the cell markers CD31 and c-kit.
- 5 2. The isolated stem cell population of claim 1 wherein at least about 75% of the cells include the cell marker CD31.
3. The isolated stem cell population of claim 1 wherein at least about 65% of the cells include the cell marker c-kit.
4. An isolated, mammalian, bone marrow-derived, lineage-negative hematopoietic stem cell population comprising endothelial progenitor cells in which at least about 80% of the cells include the CD31 cell marker and at least about 70% of the cells include the c-kit cell marker.
- 10 5. The isolated stem cell population of claim 1 wherein the cells are murine cells.
- 15 6. The isolated stem cell population of claim 1 wherein the cells are human cells.
7. The isolated stem cell population of claim 1 wherein up to about 8% of the cells also include the cell marker Sca-1 and up to about 4% of the cells also include the cell marker Flk-1/KDR.
- 20 8. The isolated stem cell population of claim 7 wherein up to about 1% of the cells include the Tie-2 cell marker.
9. An isolated, mammalian, bone marrow-derived hematopoietic stem cell population comprising endothelial progenitor cells in which about 50% to about 85% of the cells include the CD31 marker, about 70% to about 75% of the cells include the c-kit marker, about 4% to about 8% of the cells include the Sca-1 marker, and about 2% to about 4% of the cells include the Flk-1/KDR marker.
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10. The isolated stem cell population of claim 1 further including a cell culture medium.

11. The isolated stem cell population of claim 10 wherein the stem cells are derived from mammalian bone marrow.

5 12. The isolated stem cell population of claim 10 wherein the stem cells are derived from human bone marrow.

13. A method of isolating bone marrow-derived, lineage negative hematopoietic stem cells including endothelial progenitor cells comprising the steps of:

10 (a) extracting bone marrow from a mammal;
(b) separating a plurality of monocytes from the bone marrow;

(c) labeling the plurality of monocytes with biotin conjugated lineage panel antibodies to CD45, CD3, Ly-6G, CD11 and TER-119;
15 and

(d) removing monocytes that were lineage positive for CD45, CD3, Ly-6G, CD11 and TER-119 from the plurality of monocytes to provide a population of lineage negative hematopoietic stem cells including endothelial progenitor cells.

20 14. The method of claim 13 wherein the mammal is an adult mammal.

15. The method of claim 13 wherein the mammal is a mouse.

16. The method of claim 13 wherein the mammal is a human.

25 17. The method of claim 13 wherein at least about 50% of the population of lineage negative hematopoietic stem cells include a CD31 and a c-kit cell marker.

18. The method of claim 13 wherein the population of lineage negative hematopoietic stem cells includes endothelial progenitor cells capable of targeting glial enriched regions of injured adult retinas.

19. An isolated, mammalian, bone marrow-derived lineage negative hematopoietic stem cell population produced by the method of claim 13.
20. The isolated stem cell population of claim 19 wherein at least about 50% of the cells include the cell markers CD31 and c-kit.
- 5 21. The isolated stem cell population of claim 19 wherein at least about 75% of the cells include the cell marker CD31.
22. The isolated stem cell population of claim 19 wherein at least about 65% of the cells include the cell marker c-kit.
- 10 23. The isolated stem cell population of claim 19 wherein at least about 80% of the cells include the CD31 cell marker and at least about 70% of the cells include the c-kit cell marker.
24. The isolated stem cell population of claim 23 wherein up to about 8% of the cells also include the cell marker Sca-1 and up to about 4% of the cells also include the cell marker Flk-1/KDR.
- 15 25. The isolated stem cell population of claim 24 wherein up to about 1% of the cells include the Tie-2 cell marker.
26. The isolated stem cell population of claim 19 wherein about 50% to about 85% of the cells include the CD31 marker, about 70% to about 75% of the cells include the c-kit marker, about 4% to about 8% of the cells include the Sca-1 marker, and about 2% to about 4% of the cells include the Flk-1/KDR marker.
- 20 27. The isolated stem cell population of claim 19 wherein the cells are murine cells.
28. The isolated stem cell population of claim 19 wherein the cells are human cells.
- 25 29. A method of enhancing retinal neovascularization in a mammal comprising intravitreally injecting lineage negative hematopoietic stem cell population of claim 1 into the eye of a mammal in need of retinal neovasculari-

zation wherein the stem cells are derived from bone marrow of the same species of mammal as the species into whose eye the cells are injected.

30. The method of claim 29 wherein the mammal is a mouse.

31. The method of claim 29 wherein the mammal is a human.

5 32. A method of treating an ocular disease in a patient /
comprising isolating from the bone marrow of the patient a lineage negative hematopoietic stem cell population that includes endothelial progenitor cells and intravitreally injecting the isolated stem cells into an eye of the patient in a number sufficient to arrest the disease.

10 33. The method of claim 32 wherein the number of stem cells is effective for repairing retinal damage of the patient's eye.

34. The method of claim 32 wherein the number of stem cells is effective for stabilizing retinal neovasculture of the patient's eye.

15 35. The method of claim 32 wherein the number of stem cells is effective for maturing retinal neovasculture of the patient's eye.

36. The method of claim 32 wherein the population of lineage negative hematopoietic stem cells is isolated by:

- (a) extracting bone marrow from a mammal;
- (b) separating a plurality of monocytes from the bone
20 marrow;
- (c) labeling the plurality of monocytes with biotin conjugated lineage panel antibodies to CD45, CD3, Ly-6G, CD11 and TER-119; and
- (d) removing monocytes that were lineage positive for
25 CD45, CD3, Ly-6G, CD11 and TER-119 from the plurality of monocytes to provide a population of lineage negative hematopoietic stem cells including endothelial progenitor cells.

37. The method of claim 36 wherein at least about 50% of the isolated population of lineage negative hematopoietic stem cells include the cell markers CD31 and c-kit.

5 38. The method of claim 32 wherein the disease is a retinal degenerative disease.

39. The method of claim 32 wherein the disease is a retinal vascular degenerative disease.

40. The method of claim 32 wherein the disease is an ischemic retinopathy.

10 41. The method of claim 32 wherein the disease is a vascular hemorrhage.

42. The method of claim 32 wherein the disease is a vascular leakage.

15 43. The method of claim 32 wherein the disease is a choroidopathy.

44. The method of claim 32 wherein the disease is age related macular degeneration.

45. The method of claim 32 wherein the disease is diabetic retinopathy.

20 46. The method of claim 32 wherein the disease is presumed ocular histoplasmosis.

47. The method of claim 32 wherein the disease is retinopathy of prematurity.

25 48. The method of claim 32 wherein the disease is sickle cell anemia

49. The method of claim 32 wherein the disease is retinitis pigmentosa.

50. A transfected lineage negative hematopoietic stem cell population comprising a stem cell population of claim 1 transfected with a gene encoding a therapeutically useful peptide.

5 51. The transfected stem cell population of claim 50 wherein the therapeutically useful peptide is an anti-angiogenic peptide.

52. The transfected stem cell population of claim 51 wherein the anti-angiogenic peptide is a protein fragment.

53. The transfected stem cell population of claim 52 wherein the protein fragment is an anti-angiogenic fragment of TrpRS.

10 54. The transfected stem cell population of claim 53 wherein the fragment of TrpRS is T2-TrpRS.

55. A method of inhibiting retinal angiogenesis in the eye of a patient in need of retinal angiogenesis inhibition comprising intravitreally injecting a transfected stem cell population according to claim 49 into the eye of the patient.

15 56. The method of claim 55 wherein the transfected lineage negative hematopoietic stem cell population is prepared by:

- (a) extracting bone marrow from a mammal;
- (b) separating a plurality of monocytes from the bone marrow;
- 20 (c) labeling the plurality of monocytes with biotin conjugated lineage panel antibodies to CD45, CD3, Ly-6G, CD11 and TER-119; and
- (d) removing monocytes that were lineage positive for CD45, CD3, Ly-6G, CD11 and TER-119 from the plurality of monocytes to
25 provide a population of lineage negative hematopoietic stem cells including endothelial progenitor cells.

57. The method of claim 56 wherein at least about 50% of the isolated population of lineage negative hematopoietic stem cells include the cell markers CD31 and c-kit.

58. A method of delivering transgenes to the retinal vasculature of a patient comprising intravitreally injecting a transfected lineage negative hematopoietic stem cell population derived from bone marrow into the eye of the patient, wherein the stem cell population has been transfected with a therapeutically useful gene.

59. The method of claim 58 wherein the transfected lineage negative hematopoietic stem cell is prepared by:

- (a) extracting bone marrow from a mammal;
- (b) separating a plurality of monocytes from the bone marrow;
- (c) labeling the plurality of monocytes with biotin conjugated lineage panel antibodies to CD45, CD3, Ly-6G, CD11 and TER-119; and
- (d) removing monocytes that were lineage positive for CD45, CD3, Ly-6G, CD11 and TER-119 from the plurality of monocytes to provide a population of lineage negative hematopoietic stem cells including endothelial progenitor cells.

60. The method of claim 59 wherein at least about 50% of the isolated population of lineage negative hematopoietic stem cells include the cell markers CD31 and c-kit.

61. The method of claim 58 wherein the gene is useful for inhibiting retinal neovascularization.

62. A method of inducing neurotrophic rescue in a retina of a mammal suffering from a retinal degenerative disease comprising administering a neurotrophic rescue-inducing number of cells from an isolated, mammal bone-marrow-derived, lineage negative hematopoietic stem cell population containing endothelial progenitor cells to a diseased eye of the mammal; wherein at least about 50% of the stem cells include cell markers for CD31 and c-kit.

63. The method of claim 62 wherein the stem cell population is isolated by:

- (a) extracting bone marrow from a mammal;
 - (b) separating a plurality of monocytes from the bone marrow;
 - (c) labeling the plurality of monocytes with biotin conjugated lineage panel antibodies to CD45, CD3, Ly-6G, CD11 and TER-119; and
 - (d) removing monocytes that were lineage positive for CD45, CD3, Ly-6G, CD11 and TER-119 from the plurality of monocytes to provide a population of lineage negative hematopoietic stem cells including endothelial progenitor cells.
64. The method of claim 62 wherein the mammal is a human.
65. The method of claim 62 wherein the cells are administered by intravitreal injection.